DOTTORATO DI RICERCA IN BIOLOGIA CELLULARE E DELLO SVILUPPO

41 CYCLE

Project proposal for a PhD scholarship (with no financial support from Sapienza)

Title of the research: Building multi-scale modeling approaches to Pancreatic Cancer

Supervisor: *Livia Perfetto, University of Rome La Sapienza, livia.perfetto@uniroma1.it*

Host Institution: *University of Rome La Sapienza, Department of Biology and Biotechnologies 'Charles Darwin'*

Summary

Pancreatic ductal adenocarcinoma (PDAC) is characterized by a tumor microenvironment where cancer- associated fibroblast (CAFs) and cancer cells cross-talk via signals that result from the activation/repression of cell-specific signaling cascades. These processes sustain tumor growth and result in the deposition of a dense fibrotic stroma that shields the tumor from therapeutic treatments. Patient-specific proteogenomic profiling of cancer biopsies have shed light on general molecular events underlying PDAC tumorigenesis and progression but have failed to clarify the molecular mechanisms that are deregulated in individual patients. The present PhD project aims to create a multi-scale, dynamic model of PDAC tumor development and progression. It also aims to use this model to identify new therapeutic targets. This involves developing a logical modeling approach where cell populations and cell-specific pathways are represented at different organizational levels, with paracrine factors (like cytokines) serving as the connection between these levels.
The research seeks to understand the complex dynamics of PDAC tumorigenesis and progression by creating detailed, patient-specific models. These models will not only shed light on individual patient mechanisms but also help prioritize personalized therapeutic strategies for better PDAC treatment outcomes.

Pertinent Publications of the proponent (last 5 years)

1. Unveiling the signaling network of FLT3-ITD AML improves drug sensitivity prediction.
Latini S, Venafra V, Massacci G, Bica V, Graziosi S, Pugliese GM, Iannuccelli M, Frioni F, Minnella G, Marra JD, Chiusolo P, Pepe G, Helmer Citterich M, Mougiakakos D, Böttcher M, Fischer T, Perfetto L, Sacco F.
Elife. 2024. PMID: 38564252

2. Curation of causal interactions mediated by genes associated with autism accelerates the understanding of gene-phenotype relationships underlying neurodevelopmental disorders.
Iannuccelli M, Vitriolo A, Licata L, Lo Surdo P, Contino S, Cheroni C, Capocefalo D, Castagnoli L, Testa G, Cesareni G, Perfetto L.
Mol Psychiatry. 2023 PMID: 38102483

3. A key role of the WEE1-CDK1 axis in mediating TKI-therapy resistance in FLT3-ITD positive acute myeloid leukemia patients.
Massacci G, Venafra V, Latini S, Bica V, Pugliese GM, Graziosi S, Klingelhuber F, Krahmer N, Fischer T, Mougiakakos D, Boettcher M, Perfetto L, Sacco F.
Leukemia. 2023. PMID: 36509894

4. SIGNOR 3.0, the SIGnaling network open resource 3.0: 2022 update.
Lo Surdo P, Iannuccelli M, Contino S, Castagnoli L, Licata L, Cesareni G, Perfetto L.
Nucleic Acids Res. 2023. PMID: 36243968

5. A Resource to Infer Molecular Paths Linking Cancer Mutations to Perturbation of Cell Metabolism.
Iannuccelli M, Lo Surdo P, Licata L, Castagnoli L, Cesareni G, Perfetto L.
Front Mol Biosci. 2022. PMID: 35664677